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* Admitted in TX only
** Admitted in CT only

6-07-04

580/71 1648

June 4, 2004

MS Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

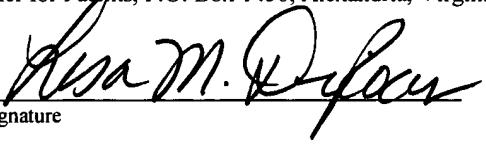
Re: U.S. Patent Application No.: 09/534717
For: *HUMAN ANTIBODIES THAT BIND HUMAN IL-12 AND METHODS FOR PRODUCING*
Inventors: Salfeld, Jochen G. *et al.*
Filed: March 24, 2000
Our Ref. No.: BBI-093CP

Dear Sir:

I enclose herewith for filing in the above-identified application the following:


1. Transmittal for Replacement Information Disclosure Statement;
2. A copy of the Information Disclosure Statement filed on February 13, 2002;
3. A copy of the Supplemental Information Disclosure Statement filed on September 23, 2003;
4. Replacement copies of each of the publications cited in the Information Disclosure Statement filed on February 13, 2002;
5. Replacement copies of each of the publications cited in the Information Disclosure Statement filed on September 23, 2003;
6. Second Supplemental Information Disclosure Statement;
7. PTO Form SB/08;
8. Copies of the publication cited in PTO Form SB/08 (1);
9. A Copy of the Taiwanese Office Action dated May 4, 2004; and
10. A Return Postcard.

No additional costs are believed to be due in connection with the filing of this Information Disclosure Statement. However, please charge any necessary fees in connection with the enclosed statement to our Deposit Order Account No. 12-0080. For this purpose, a duplicate of this sheet is attached.

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|---|
| "Express Mail" Mailing Label Number <u>EV 378819459 US</u> |
| Date of Deposit <u>June 4, 2004</u> |
| I hereby certify that this transmittal letter and the papers referred to as being enclosed therein are being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to MS Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450 |
|  Signature |
| <u>Lisa M. DiRocco, Esq.</u> |

Respectfully submitted,

LAHIVE & COCKFIELD, LLP


Lisa M. DiRocco, Esq.
Registration No. 51,619
Attorney for Applicants



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the application of: Jochen Salfeld *et al.*

Serial No.: 09/534,717

Filed: March 24, 2000

For: *HUMAN ANTIBODIES THAT BIND HUMAN IL-12 AND METHODS FOR PRODUCING*

Docket No.: BBI-093CP

Group Art Unit: 1647

Examiner: F. Hamud

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

CERTIFICATION UNDER 37 CFR 1.10

Date of Deposit: June 4, 2004

Mailing Label Number: EV378819459US

I hereby certify that this 37 CFR 1.53(d) request and the documents referred to therein as enclosed are being deposited with the United States Postal Service on the date indicated above in an envelope as "Express Mail Post Office to Addressee" service under 37 CFR 1.10 and addressed to Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

Lisa M. DiRocco, Esq.

Name of Person Mailing Paper

Signature of Person Mailing Paper

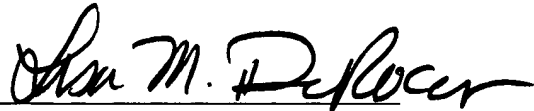
**TRANSMITTAL FOR REPLACEMENT INFORMATION DISCLOSURE
STATEMENTS**

Dear Sir:

In response to the Examiner's request, Applicants enclose herewith copies of the Information Disclosure Statement filed on February 13, 2002 and the Supplemental Information Disclosure Statement filed on September 23, 2003, in the above-referenced application. Also enclosed herewith are replacement copies of each of the publications cited in the Information Disclosure Statement filed on February 13, 2002 and the Supplemental Information Disclosure Statement filed on September 23, 2003, for the Examiner's consideration.

It is Applicants' understanding that no fees are associated with the submission of these replacement Information Disclosure Statements and replacement copies of publications cited therein. However, please charge any necessary fees associated with this communication to our Deposit Account No. 12-0080. Applicants request any extensions of time necessary to respond.

Respectfully submitted,
LAHIVE & COCKFIELD, LLP

A handwritten signature in black ink, appearing to read "Lisa M. DiRocco", written over a horizontal line.

Lisa M. DiRocco, Esq.
Registration No. 51,619
Attorney for Applicants

28 State Street
Boston, MA 02109
(617) 227-7400

Date: June 4, 2004

Enclosures



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the application of: Salfeld, Jochen G. *et al.*

Serial No.: 09/534717

Filed: March 24, 2000

For: *HUMAN ANTIBODIES THAT BIND HUMAN
IL-12 AND METHODS FOR PRODUCING*

Attorney Docket No.: BBI-093CP

Group Art Unit: 1647

Examiner: Hamud, Fozia M.

MS Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

"Express Mail" mailing label number: EV378819459US

Date of Deposit: June 4, 2004

I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to MS Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

Signature

Lisa M. DiRocco, Esq.

Please Print Name of Person Signing

SECOND SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Dear Sir:


Applicants and their Attorney have become aware of the following publication and information, cited in a Taiwanese Office Action mailed May 4, 2004 during the prosecution of TW 89105501 which corresponds to the above referenced application. In accordance with 37 CFR §1.97, Applicants hereby submit this publication for the Examiner's consideration. This publication is cited on the enclosed PTO Form SB/08, and a copy of the Office Action and the publication cited thereon are enclosed as well.

This statement is not to be interpreted as a representation that the cited publications are material, that an exhaustive search has been conducted, or that no other relevant information exists. Nor shall the citation of any publication herein be construed *per se* as a representation that such publication is prior art. Moreover, the Applicants understand that the Examiner will make an independent evaluation of the cited publications.

In accordance with 37 CFR §1.97(e)(1), the undersigned hereby certifies that each item contained in this Supplemental Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart foreign application *for the first time* not more than three months prior to the filing of this statement. Furthermore, in accordance with 37 CFR §1.704(d), Applicants note that this communication was not received by any individual designated in §1.56(c) more than thirty days prior to the filing of this statement.

No additional costs are believed to be due in connection with the filing of this Supplemental Information Disclosure Statement. However, please charge any necessary fees in connection with the enclosed statement to our Deposit Order Account No. 12-0080.

Respectfully submitted,
LAHIVE & COCKFIELD, LLP



Lisa M. DiRocco, Esq.
Registration No. 51,619
Attorney for Applicants

28 State Street
Boston, MA 02109
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Date: June 4, 2004

GAD/EAH/LMD/kvj
Enclosures



PTO/SB/08a/b (08-03)
Approved for use through 07/31/2006. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

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|---|---|----|---|--------------------------|--------------------|
| Substitute for form 1449A/B/PTO SECOND SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use as many sheets as necessary) | | | | Complete if Known | |
| | | | | Application Number | BBI-093CP |
| | | | | Filing Date | March 24, 2000 |
| | | | | First Named Inventor | Salfeld, Jochen G. |
| | | | | Art Unit | 1647 |
| | | | | Examiner Name | Hamud, Fozia M. |
| Sheet | 1 | of | 1 | Attorney Docket Number | BBI-093CP |

| U.S. PATENT DOCUMENTS | | | | | |
|-----------------------|--------------------------|--|--------------------------------|--|---|
| Examiner Initials* | Cite No. ¹ | Document Number | Publication Date MM-DD-YYYY | Name of Patentee or Applicant of Cited Document | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear |
| | | Number-Kind Code ² (if known) | | | |
| | | | | | |

| FOREIGN PATENT DOCUMENTS | | | | | | |
|--------------------------|--------------------------|---|-----------------------------------|--|---|----------------|
| Examiner Initials* | Cite No. ¹ | Foreign Patent Document | Publication Date MM-DD-YYYY | Name of Patentee or Applicant of Cited Document | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear | T ⁶ |
| | | Country Code ³ -Number ⁴ -Kind Code ⁵ (if known) | | | | |
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*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

| NON PATENT LITERATURE DOCUMENTS | | | |
|---------------------------------|--------------------------|---|----------------|
| Examiner Initials* | Cite No. ¹ | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published. | T ² |
| | G1 | Jackson, J.J. <i>et al.</i> "In vitro maturation: improvement of a high affinity, neutralizing antibody against IL-1 β ." <i>The Journal of Immunology</i> 154(7):3310-19 (1995). | |

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Applicant's unique citation designation number (optional). ² Applicant is to place a check mark here if English language Translation is attached.

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| Examiner Signature | | Date Considered | |
|-----------------------|--|--------------------|--|

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Office No. BBI-093CP

**THE "RECEIVED" STAMP OF THE PATENT AND TRADEMARK OFFICE
IMPRINTED HEREON ACKNOWLEDGES THE FILING OF:**

Description of Paper* : Transmittal Letter (in duplicate), Information Disclosure Statement, PTO Form 1449 and copies of all publications cited therein (56) are enclosed along with this postcard.

Title: *HUMAN ANTIBODIES THAT BIND HUMAN IL-12 AND METHODS FOR PRODUCING*

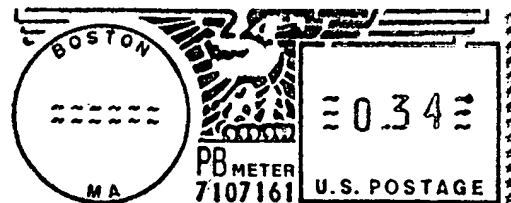
Name of Applicants: Jochen Salfeld *et al.*

Serial No.: 09/534,717

Atty: Elizabeth A. Hanley, Esq./CEH

Date: February 13, 2002

*with Certificate of First Class Mailing



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MERIDETH C. ARNOLD

* Admitted in NY only
** Passed the Patent Bar Examination
*** Admitted in TX only

Commissioner for Patents
Washington, D.C. 20231

Re: U.S. Patent Application No.: 09/534,717
Title: *HUMAN ANTIBODIES THAT BIND HUMAN IL-12
AND METHODS FOR PRODUCING*
Inventors: Jochen Salfeld *et al.*
Filed: March 24, 2000
Our Ref. No.: BBI-093CP

Dear Sir:

I enclose herewith for filing in the above-identified application the following:

1. Information Disclosure Statement;
2. PTO Form 1449;
3. Copies of references cited in PTO Form 1449; and
4. A Return Postcard.

No additional costs are believed to be due in connection with the filing of this Information Disclosure Statement. However, please charge any necessary fees in connection with the enclosed statement to our Deposit Order Account No. 12-0080. For this purpose, a duplicate of this sheet is attached.

I hereby certify that this correspondence is deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, Washington, D.C. 20231 on:

Date

Elizabeth A. Hanley, Esq Reg. No. 33,505

Respectfully submitted,
LAHIVE & COCKFIELD, LLP

Elizabeth A. Hanley, Esq.
Registration No. 33,505
Attorney for Applicants

COPY AS FILED
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the application of: Jochen Salfeld *et al.*

Serial No.: 09/534,717

Filed: March 24, 2000

For: *HUMAN ANTIBODIES THAT BIND HUMAN
IL-12 AND METHODS FOR PRODUCING*

Docket No.: BBI-093CP

Group Art Unit: 1646

Examiner: Prasad, S.

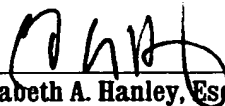
Commissioner for Patents
Washington, D.C. 20231

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2/13/02
Date of Signature and of Mail Deposit

By:


Elizabeth A. Hanley, Esq.
Registration No. 33,505
Attorney for Applicants

INFORMATION DISCLOSURE STATEMENT

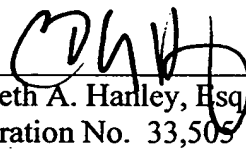
Dear Sir:

Applicants and their attorney are aware of the following publications and information, listed on the attached PTO Form 1449, and in accordance with 37 C.F.R. §1.97 hereby submit these publications for the Examiner's consideration. A copy of each cited publication is enclosed.

This statement is not to be interpreted as a representation that the cited publications are material, that an exhaustive search has been conducted, or that no other relevant information exists. Nor shall the citation of any publication herein be construed *per se* as a representation that such publication is prior art. Moreover, Applicants understand that the Examiner will make an independent evaluation of the cited publications.

Under 37 CFR § 1.97(b)(3), no additional costs are believed to be due in connection with the filing of this disclosure. If, however, a first Office Action on the merits issues in this application bearing a mailing date prior to the date of this Information Disclosure Statement, please charge the appropriate fee as required under 37 CFR §1.17(p) to our Deposit Order Account No. 12-0080.

Respectfully submitted,
LAHIVE & COCKFIELD, LLP


Elizabeth A. Hanley, Esq.
Registration No. 33,505
Attorney for Applicants

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Date: _____

2/13/02

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Enclosures

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|--|---|---|---------------------------------|
| APPLICANT FACSIMILE OF FORM PTO-1449 REV 7-80 | U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE | ATTY DOCKET NO BBI-093CP | SERIAL NO 009/534,717 |
| LIST OF PUBLICATIONS CITED BY APPLICANT (Use several sheets if necessary) | | APPLICANT Jochen Salfeld et al. | |
| | | FILING DATE March 24, 2000 | GROUP 1646 |

U.S. PATENT DOCUMENTS

| EXAMINER INITIAL | | DOCUMENT NUMBER | DATE | NAME | CLASS | SUBCLASS | FILING DATE IF APPROPRIATE |
|---------------------|----|-----------------|------|-------------|-------|----------|-------------------------------|
| | A1 | 4,816,397 | 3/89 | Boss et al. | 435 | 68 | |
| | A2 | 5,658,754 | 8/97 | Kawasaki | 435 | 69.1 | |
| | A3 | 5,643,768 | 7/97 | Kawasaki | 435 | 91.21 | |

FOREIGN PATENT DOCUMENTS

| | | DOCUMENT NUMBER | DATE | COUNTRY | CLASS | SUBCLASS | TRANSLATION YES NO | |
|--|----|-----------------|------|---------|-------|----------|-----------------------|--|
| | A4 | WO 9404679 A1 | 3/94 | PCT | | | | |
| | A5 | EP 0 659 766 A1 | 6/95 | EPO | | | | |
| | A6 | WO 9524918 A1 | 9/95 | PCT | | | | |

OTHERS (including Author, Title, Date, Pertinent Pages, Etc.)

| | | |
|--|-----|--|
| | A7 | Balashov KE, et al. Increased interleukin 12 production in progressive multiple sclerosis: induction by activated CD4+ T cells via CD40 ligand. Proc Natl Acad Sci U S A. 1997 Jan 21;94(2):599-603 |
| | A8 | Barbas CF 3rd, et al. Assembly of combinatorial antibody libraries on phage surfaces: the gene III site. Proc Natl Acad Sci U S A. 1991 Sep 15;88(18):7978-82 |
| | A9 | Berrebi D, et al. Interleukin-12 expression is focally enhanced in the gastric mucosa of pediatric patients with Crohn's disease. Am J Pathol. 1998 Mar;152(3):667-72 |
| | A10 | Bird RE, et al. Single-chain antigen-binding proteins. Science. 1988 Oct 21;242(4877):423-6 |
| | A11 | Brown PS Jr, et al. Anti-Tac-H, a humanized antibody to the interleukin 2 receptor, prolongs primate cardiac allograft survival. Proc Natl Acad Sci U S A. 1991 Apr 1;88(7):2663-7 |
| | A12 | Bucht A, et al. Expression of interferon-gamma (IFN-gamma), IL-10, IL-12 and transforming growth factor-beta (TGF-beta) mRNA in synovial fluid cells from patients in the early and late phases of rheumatoid arthritis (RA). Clin Exp Immunol. 1996 Mar;103(3):357-67 |
| | A13 | Carter RW, et al. "Production and characterization of monoclonal antibodies to human interleukin-12," Hybridoma. 1997 Aug;16(4):363-9 |
| | A14 | Clackson T, et al. Making antibody fragments using phage display libraries. Nature. 1991 Aug 15;352(6336):624-8 |
| | A15 | Dall'Acqua W, et al. Antibody engineering. Curr Opin Struct Biol. 1998 Aug;8(4):443-50 |
| Examiner | | Date Considered |
| EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. | | |

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|--|---|---|--------------------------|
| APPLICANT FACSIMILE OF FORM PTO-1449 REV 7-80 | U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE | ATTY DOCKET NO BBI-093CP | SERIAL NO. 09/533,717 |
| LIST OF PUBLICATIONS CITED BY APPLICANT (Use several sheets if necessary) | | APPLICANT Jochen Salfeld et al. | |
| | | FILING DATE March 24, 2000 | GROUP 1646 |

OTHERS (including Author, Title, Date, Pertinent Pages, Etc.)

| | | |
|--|-----|--|
| | B1 | Fais S, et al. Interferon expression in Crohn's disease patients: increased interferon-gamma and -alpha mRNA in the intestinal lamina propria mononuclear cells. J Interferon Res. 1994 Oct;14(5):235-8 |
| | B2 | Fuchs P, et al. Targeting recombinant antibodies to the surface of Escherichia coli: fusion to a peptidoglycan associated lipoprotein. Biotechnology (N Y). 1991 Dec;9(12):1369-72 |
| | B3 | Fuss IJ, et al. Disparate CD4+ lamina propria (LP) lymphokine secretion profiles in inflammatory bowel disease. Crohn's disease LP cells manifest increased secretion of IFN-gamma, whereas ulcerative colitis LP cells manifest increased secretion of IL-5. J Immunol. 1996 Aug 1;157(3):1261-70 |
| | B4 | Gately MK, et al. The interleukin-12/interleukin-12-receptor system: role in normal and pathologic immune responses. Annu Rev Immunol. 1998;16:495-521 |
| | B5 | Garrard LJ, et al. F _{ab} assembly and enrichment in a monovalent phage display system. Biotechnology (N Y). 1991 Dec;9(12):1373-7 |
| | B6 | Gram H, et al. In vitro selection and affinity maturation of antibodies from a naive combinatorial immunoglobulin library. Proc Natl Acad Sci U S A. 1992 Apr 15;89(8):3576-80 |
| | B7 | Griffiths AD, et al. Human anti-self antibodies with high specificity from phage display libraries. EMBO J. 1993 Feb;12(2):725-34 |
| | B8 | Hanes J, et al. In vitro selection and evolution of functional proteins by using ribosome display. Proc Natl Acad Sci U S A. 1997 May 13;94(10):4937-42 |
| | B9 | Hawkins RE, et al. Selection of phage antibodies by binding affinity. Mimicking affinity maturation. J Mol Biol. 1992 Aug 5;226(3):889-96 |
| | B10 | Hay BN, et al. Bacteriophage cloning and Escherichia coli expression of a human IgM Fab. Hum Antibodies Hybridomas. 1992 Apr;3(2):81-5 |
| | B11 | Duchmann et al., Tolerance towards resident intestinal flora in mice is abrogated in experimental colitis and restored by treatment with interleukin-10 or antibodies to interleukin-12. Eur. J. Immunol. 1996, 26:934-8 (Abstract) |
| | B12 | Hoogenboom HR, et al. Multi-subunit proteins on the surface of filamentous phage: methodologies for displaying antibody (Fab) heavy and light chains. Nucleic Acids Res. 1991 Aug 11;19(15):4133-7 |
| | B13 | He M, et al. Antibody-ribosome-mRNA (ARM) complexes as efficient selection particles for in vitro display and evolution of antibody combining sites. Nucleic Acids Res. 1997 Dec 15;25(24):5132-4 |
| | B14 | Huse WD, et al. Generation of a large combinatorial library of the immunoglobulin repertoire in phage lambda. Science. 1989 Dec 8;246(4935):1275-81 |
| Examiner | | Date Considered |
| EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. | | |

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| | | FILING DATE March 24, 2000 | GROUP 1646 |

OTHERS (including Author, Title, Date, Pertinent Pages, Etc.)

| | |
|--|--|
| C1 | Huston JS, et al. Protein engineering of antibody binding sites: recovery of specific activity in an anti-digoxin single-chain Fv analogue produced in Escherichia coli. Proc Natl Acad Sci U S A. 1988 Aug;85(16):5879-83 |
| C2 | Irving RA, et al. Affinity maturation of recombinant antibodies using E. coli mutator cells, Immunotechnology. 1996 Jun;2(2):127-43 |
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| APPLICANT FACSIMILE OF FORM PTO-1449 REV 7-80 LIST OF PUBLICATIONS CITED BY APPLICANT (Use several sheets if necessary) | U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE | ATTY DOCKET NO BBI-093CP | SERIAL NO. 09/534,717 |
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FOREIGN PATENT DOCUMENTS

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